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REMARKS

Claims 1-12 and 20-22 are presented for examination. Claims 13-19 have been withdrawn. Claims 1, 3, 5-7, 9, and 11 have been amended, and Claims 20-22 have been added. Support for the amendments to Claims 1, 3, 5-7, 9, and 11 can be found throughout the specification, such as on page 4, lines 14-28, and Figures 1-3 for example. Support for Claims 20-22 can be found on page 3, lines 26-31. Accordingly, no new matter has been added by these amendments.

Rejections Under 35 U.S.C §112, Second Paragraph

Claims 5 and 6 stand rejected under 35 U.S.C. §112, second paragraph for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the sole interest of expediting the prosecution of this case, Claims 5 and 6 have been amended to no longer recite the term "said bases". Accordingly, Applicants respectfully request the withdrawal of this rejection.

Rejections Under 35 U.S.C §112, First Paragraph

Claims 1-12 stand rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

To satisfy the written description requirement, a patent application must describe the invention in sufficient detail that one of skill in the relevant art could conclude that the inventor was in possession of the claimed invention at the time the application was filed. *See Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, (Fed. Cir. 1991). According to the Federal Circuit, it is clear that Applicants need not precisely recite each and every element of a claim limitation in the specification in order to satisfy the written description requirement. *See Union Oil of Cal. v. Atlantic Richfield Co.*, 208 F.3d 989 (Fed. Cir. 2000).

The Examiner asserts that the specification does not disclose any distinguishing identifying characteristics of the claimed antisense oligonucleotides, that would complement at

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least two RNA molecules of different sequence and function as an antisense oligonucleotide against both, which would indicate that applicant was in possession of the claimed genus.

Applicants respectfully disagree. It is first noted that the claims have been amended to recite antisense oligonucleotides and ribozymes that hybridize to at least two RNA molecules that differ in sequence by at least one nucleotide mismatch, and wherein a degenerate or universal base is positioned on said oligonucleotide or ribozyme to correspond to said nucleotide mismatch. Support for the amended claims can be found throughout the specification, such as on page 4, lines 14-28, and Figures 1-3 for example. As described in the specification, the claimed antisense molecules are an important advancement over the prior art as they can bind with sufficient affinity to multiple targets having mismatched oligonucleotides.

Sequences of the claimed antisense molecules can be found throughout the specification. For example, pages 9-10 of the specification provide the structure of 11 antisense oligonucleotides.

5'-NNN NNN BBB BBB NNN NNN-3' (SEQ ID NO: 1)
5'-NNN NNN BBB BBB NNN NNN-3' (SEQ ID NO: 2)
5'-NNN NNN BBB BBB NNN NNN-3' (SEQ ID NO: 3)
5'-NNN NNN BBB BBB NNN NNN-3' (SEQ ID NO: 4)
5'-NNN BNN BBN BNB NBN NBN-3' (SEQ ID NO: 5)
5'-NNN BNN BBN BNB NBN NBN-3' (SEQ ID NO: 6)
5'-NNN BNN BBN BNB NBN NBN-3' (SEQ ID NO: 7)
5'-a*a*a*a*-----NNN BNN BBN BNB NBN NBN-3' (SEQ ID NO: 8)
5'-NNN BNN BBN#BNB NBN NBN-3' (SEQ ID NO: 9)
5'-NNN BNN BBN&BNB NBN NBN-3' (SEQ ID NO: 10)
5'-NNN BNN BBN BNB NBN NBN-3' (SEQ ID NO: 11)

Additionally, Example 3 on page 13 of the specification describes a specific antisense oligonucleotide against PKC α : 5'-GTTCTCXXXXXXGAGTTT-3' (SEQ ID NO: 17). Example 4, on page 14 of the specification describes an antisense oligonucleotide directed to a Bcl2 target:

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5'-TCTXCCXXCXTXCXCCXT-3' (SEQ ID NO: 19). Example 8, on pages 17 and 18, describes three antisense oligonucleotides against bcl-2: 3'-GGGCCPGTGTGPGKGGTA (SEQ ID NO: 26), 3'-CGTCTGKGGCCGACGGKGG (SEQ ID NO: 28), and 3'-GGCPGPGGPGGCCCPG (SEQ ID NO: 30).

In addition, Figure 1 provides six different examples of the antisense oligonucleotides that bind to two different bcl targets (bcl-2A and bcl-xL). Similarly, Figure 2 provides nine specific examples of antisense oligonucleotides that bind to various PKC targets (PKCa, PKCt, and PKCd). Figure 3 discloses 15 different examples of antisense oligonucleotides that bind to two different bcl targets (bcl-2B and bcl-2C). Each of the afore-mentioned 43 antisense oligonucleotides hybridize to at least two RNA molecules that differ in sequence by at least one nucleotide mismatch and at least one degenerate or universal base in each of these antisense oligonucleotides is positioned to correspond to a nucleotide mismatch on the RNA target such that the antisense oligonucleotides can bind to the two RNAs.

Accordingly, Applicants have disclosed a total of 46 examples of the claimed antisense oligonucleotides by sequence and therefore by structure, thus satisfying the "precise definition" requirements of *Univ. of Rochester*. Furthermore, Applicants submit that 46 examples of claimed embodiments is more than sufficient to satisfy the "representative number to satisfy a genus" requirement set forth in *Eli Lilly & Co.* Applicants respectfully submit that the now pending claims satisfy the written description requirement set forth in 35 U.S.C. § 112, as interpreted by the Federal Circuit, and are consistent with current policy at the United States Patent and Trademark Office. Thus, Applicants request withdrawal of the rejections under 35 U.S.C. § 112.

Rejections Under 35 U.S.C. § 102

A reference must teach each and every element to anticipate a claim under 35 U.S.C. § 102. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). "Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. ...There must be no difference between the claimed invention

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and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention.”
See Scripps Clinic & Research Foundation v. Genentech, Inc., 927 F.2d 1565 (Fed. Cir. 1991).

Claims 1-8 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Cook et al. (U.S Patent No. 5,623,065). As discussed above, the now pending claims recite antisense oligonucleotides and ribozymes that hybridize to at least two RNA molecules that differ in sequence by at least one nucleotide mismatch, and wherein a degenerate or universal base is positioned on said oligonucleotide or ribozyme to correspond to said nucleotide mismatch. As Cook et al. does not teach an antisense oligonucleotide having a degenerate or universal base positioned to correspond to a nucleotide mismatch on a target sequence, Applicants respectfully request the withdrawal of this rejection.

Claims 1, 2, and 4-8 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Torrence et al. (U.S Patent No. 5,583,032). As discussed above, the claims have been amended to recite antisense oligonucleotides and ribozymes that hybridize to at least two RNA molecules that differ in sequence by at least one nucleotide mismatch, and wherein a degenerate or universal base is positioned on said oligonucleotide or ribozyme to correspond to said nucleotide mismatch. As Torrence et al. does not teach an antisense oligonucleotide having a degenerate or universal base positioned to correspond to a nucleotide mismatch on a target sequence, Applicants respectfully request the withdrawal of this rejection.

Claims 1, 2, 7, 8, 11, and 12 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Stinchcomb et al. (U.S Patent No. 5,646,042). As discussed above, the now pending claims recite antisense oligonucleotides and ribozymes that hybridize to at least two RNA molecules that differ in sequence by at least one nucleotide mismatch, and wherein a degenerate or universal base is positioned on said oligonucleotide or ribozyme to correspond to said nucleotide mismatch. As Stinchcomb et al. does not teach an antisense oligonucleotide or ribozyme having

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a degenerate or universal base positioned to correspond to a nucleotide mismatch on a target sequence, Applicants respectfully request the withdrawal of this rejection.

Claims 1-6 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Bennett et al. (U.S. Patent No. 6,172,216). As discussed above, the claims have been amended to recite antisense oligonucleotides and ribozymes that hybridize to at least two RNA molecules that differ in sequence by at least one nucleotide mismatch, and wherein a degenerate or universal base is positioned on said oligonucleotide or ribozyme to correspond to said nucleotide mismatch. As Bennet et al. does not teach an antisense oligonucleotide having a degenerate or universal base positioned to correspond to a nucleotide mismatch on a target sequence, Applicants respectfully request the withdrawal of this rejection. Applicants respectfully submit that the now pending claims are novel over the cited art and request the withdrawal of all rejections under 35 U.S.C. §102.

Rejection Under 35 U.S.C. § 103

Claims 7-12 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Werther et al. (US Patent 5,929,040) in view of Bennett et al., Torrence et al., and Krupp (1993, reference 82, PTO-1449 filed 8/28/02). Applicants respectfully disagree.

To establish a *prima facie* case of obviousness a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success found in the prior art. Third, the prior art must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

Applicants respectfully submit that the cited art fails to teach or suggest all of the claim limitations. As discussed above, the claims have been amended to recite antisense oligonucleotides and ribozymes that hybridize to at least two RNA molecules that differ in sequence by at least one nucleotide mismatch, and wherein a degenerate or universal base is

positioned on said oligonucleotide or ribozyme to correspond to said nucleotide mismatch. The cited references alone or in combination do not teach, suggest, or motivate one of skill in the art to make an antisense oligonucleotide or ribozyme having a degenerate or universal base positioned to correspond to a nucleotide mismatch on a target sequence. Accordingly, Applicants respectfully request the withdrawal of this rejection and allowance of the pending claims.

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the claims, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. Any claim amendments which are not specifically discussed in the above remarks are made in order to improve the clarity of claim language, to correct grammatical mistakes or ambiguities, and to otherwise improve the capacity of the claims to particularly and distinctly point out the invention to those of skill in the art. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is specifically requested.

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